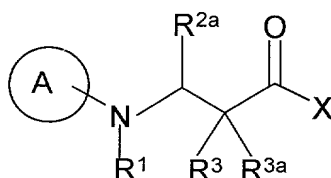


WHAT IS CLAIMED IS:

1. A compound of Formula (I):



(I)

wherein:

R¹ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted alkenyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R³ and R^{3a} are independently selected from the group consisting of hydrogen, halogen, alkyl, substituted alkyl, alkenyl, alkynyl, alkoxy, haloalkoxy, alkylthio, or -(Alk^b)_mR^b in which Alk^b is a C₁₋₃alkylene chain, m is 0 or 1 and R^b is hydroxy, thiol, nitro, cyano, carboxy, -CO₂R^c (wherein R^c is alkyl), -SO₃H, -SOR^c, -SO₂R^c, -SO₃R^c, -OCO₂R^c, -C(O)H, -COR^c, -OCOR^c, -CSR^c, -NR^dR^e (wherein R^d and R^e are independently hydrogen, alkyl, or substituted alkyl), -CONR^dR^e, -OCONR^dR^e, -NR^dCOR^e, -CSNR^dR^e, -NR^dCSR^e, -SO₂NR^dR^e, -NR^dSO₂R^e, -NR^dCONR^eR^f (where R^f is hydrogen alkyl, or substituted alkyl) or -NR^dSO₂NR^eR^f;

X is selected from the group consisting of hydroxyl, alkoxy, substituted alkoxy, alkenoxy, substituted alkenoxy, cycloalkoxy, substituted cycloalkoxy, cycloalkenox, substituted cycloalkenox, aryloxy, substituted aryloxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy and -NR^{''}R^{''} where each R^{''} is independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkenyl, substituted

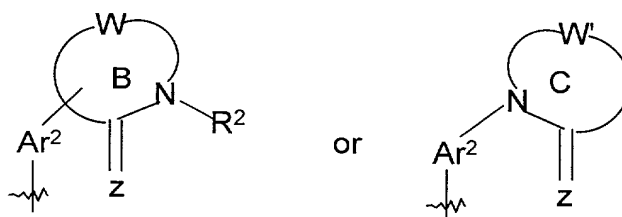
alkenyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

A is an aryl, heteroaryl, cycloalkyl, or heterocyclic group wherein said aryl, heteroaryl, cycloalkyl, or heterocyclic group is optionally substituted,
5 on any ring atom capable of substitution, with 1-3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, acyl, acylamino, thiocarbonylamino, acyloxy, amino, substituted amino, amidino, alkyl amidino, thioamidino, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, aryl, substituted aryl, aryloxy, substituted aryloxy, aryloxyaryl, substituted aryloxyaryl, cyano, halogen,
10 hydroxyl, nitro, oxo, carboxyl, cycloalkyl, substituted cycloalkyl, guanidino, guanidinosulfone, thiol, thioalkyl, substituted thioalkyl, thioaryl, substituted thioaryl, thiocycloalkyl, substituted thiocycloalkyl, thioheteroaryl, substituted thioheteroaryl, thioheterocyclic, substituted thioheterocyclic, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic, cycloalkoxy, substituted cycloalkoxy, heteroaryloxy, substituted heteroaryloxy, heterocyclyloxy, substituted heterocyclyloxy, oxycarbonylamino, oxythiocarbonylamino, -OS(O)₂-alkyl, -OS(O)₂-substituted alkyl, -OS(O)₂-aryl, -OS(O)₂-substituted aryl, -OS(O)₂-heteroaryl, -OS(O)₂-substituted
15 heteroaryl, -OS(O)₂-heterocyclic, -OS(O)₂-substituted heterocyclic, -OSO₂-NRR where each R is independently hydrogen or alkyl, -NRS(O)₂-alkyl, -NRS(O)₂-substituted alkyl, -NRS(O)₂-aryl, -NRS(O)₂-substituted aryl, -NRS(O)₂-heteroaryl, -NRS(O)₂-substituted heteroaryl, -NRS(O)₂-heterocyclic, -NRS(O)₂-substituted heterocyclic, -NRS(O)₂-NR-alkyl, -NRS(O)₂-NR-substituted alkyl, -NRS(O)₂-NR-aryl, -NRS(O)₂-NR-substituted
20 aryl, -NRS(O)₂-NR-heteroaryl, -NRS(O)₂-NR-substituted heteroaryl, -NRS(O)₂-NR-heterocyclic, -NRS(O)₂-NR-substituted heterocyclic where R is hydrogen or alkyl, -N[S(O)₂-R']₂ and -N[S(O)₂-NR']₂ where each R' is independently selected from the group consisting of alkyl, substituted alkyl,

aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

R^{2a} is either:

- (i) an $-Ar^1-R^9$ group where Ar^1 is aryl or heteroaryl optionally substituted with one or two substituents selected from the group consisting of hydroxy, acyl, acylamino, aminoacyl, acyloxy, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, aminoacyl, aminocarbonyloxy, carboxyl, carboxylalkyl, carboxylamido, cyano, thiol, thioalkyl, substituted thioalkyl, halo, nitro provided that said acyl, acylamino, acyloxy, substituted alkyl, substituted alkoxy and substituted thioalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; and R^9 is selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocarbonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino and oxysulfonyl provided that when R^9 is acylamino or acyloxy then the acylamino or acyloxy group does not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; or
- (ii) a group of formula (a) or (b):



wherein:

Ar^2 is an aryl or heteroaryl group optionally substituted, in addition to ring B or C, with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino,

substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, and substituted alkylsulfonyl;

10 Z is -O- or -S-;

 B is a group wherein W, together with -C(=Z)NR²-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and -SO_n- (where n is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, alkylene dioxy, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl,

substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl;

R² is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, and substituted cycloalkenyl;

C is a group wherein W', together with -C(=Z)N-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and -SO_n- (where n is 0 to 2) wherein said saturated or unsaturated

heterocyclic group is optionally fused with one or two ring(s) structures selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group

consisting of with one or two substituent(s) selected from the group consisting of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, alkylenedioxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino,

substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, nitro, acyl, substituted acyl, carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted

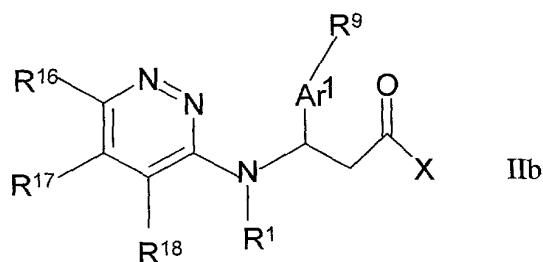
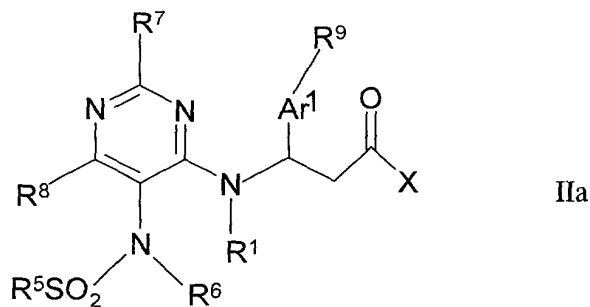
alkylsulfonyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl; or (iii) HetAr where HetAr is a nitrogen containing heteroaryl that is optionally substituted with an aryl or substituted aryl group;

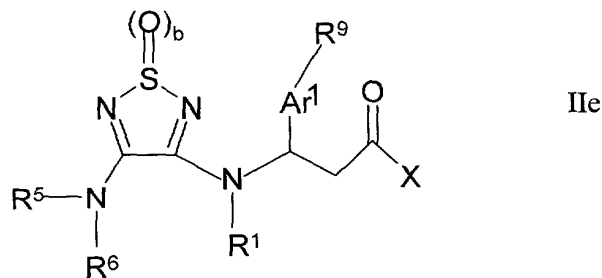
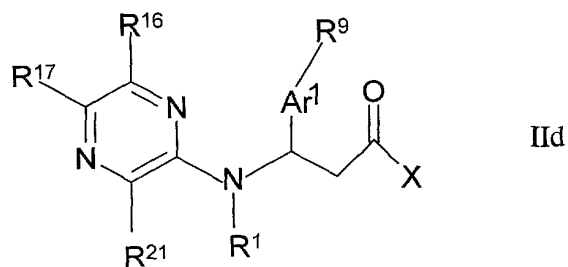
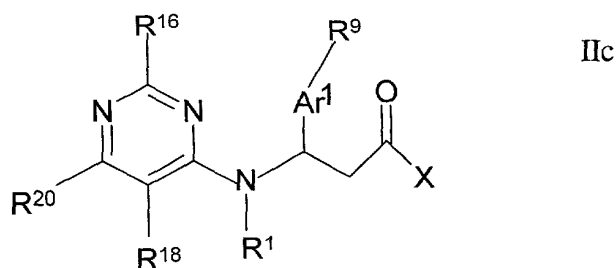
and enantiomers, diastereomers and pharmaceutically acceptable salts thereof;

and further wherein the compound of Formula I has a binding affinity to VLA-4 as expressed by an IC_{50} of about $15\mu M$ or less.

2. The compound of Claim 1 wherein R^{2a} is an $-Ar^1-R^9$ group wherein Ar^1 and R^9 are as defined above.
3. The compound of Claim 1 wherein Ar^1 is phenyl with the R^9 in the *para* position of the phenyl ring.
4. The compound of Claim 3 wherein R^9 is selected from the group consisting of $-O-Z^a-NR^{11}R^{11'}$ and $-O-Z^a-R^{12}$ wherein R^{11} and $R^{11'}$ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R^{11} and $R^{11'}$ are joined to form a heterocycle or a substituted heterocycle, R^{12} is selected from the group consisting of heterocycle and substituted heterocycle, and Z^a is selected from the group consisting of $-C(O)-$ and $-SO_2-$.
5. The compound of Claim 4 wherein R^9 is $-OC(O)NR^{11}R^{11'}$.
6. The compound of Claim 1 wherein Ar^1 is phenyl with a $-OCON(CH_3)_2$ group at the *para* position of the phenyl ring.
7. The compound of Claim 1 wherein A in the above compounds is heteroaryl optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.

8. The compound of Claim 1 wherein A is selected from the group consisting of 1-oxo-1,2,5-thiadiazole, 1,1-dioxo-1,2,5-thiadiazole, pyridazine, pyrimidine or pyrazine wherein said rings are optionally substituted with 1 to 3 substituents selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen.
9. The compound of Claims 1-8 wherein R^1 , R^3 and R^{3a} are hydrogen, and X is hydroxyl.
10. The compound of Claim 1 wherein the compound has formula IIa, IIb, IIc, IId or IIe:





wherein X is hydroxy or alkoxy;

R¹ is hydrogen;

R⁵ is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R⁶ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and -SO₂R¹⁰ where R¹⁰ is selected from the

group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

5 R^7 and R^8 are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

10 R^{16} and R^{17} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

15 R^{18} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

20 R^{20} is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R^{21} is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2;

25 Ar^1 is aryl or heteroaryl optionally substituted with one or two substituents selected from the group consisting of hydroxy, acyl, acylamino, acyloxy, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, aminoacyl, aminocarbonyloxy, carboxyl, carboxylalkyl, carboxylamido, cyano, thiol, thioalkyl, substituted thioalkyl, halo, nitro provided that said
30 acyl, acylamino, acyloxy, substituted alkyl, substituted alkoxy and substituted

thioalkyl do not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group; and

R⁹ is selected from the group consisting of acyl, acylamino, acyloxy, aminoacyl, aminocarbonylamino, aminothiocabonylamino, aminocarbonyloxy, oxycarbonylamino, oxythiocarbonylamino, thioamidino, thiocarbonylamino, aminosulfonylamino, aminosulfonyloxy, aminosulfonyl, oxysulfonylamino and oxysulfonyl provided that when R⁹ is acylamino or acyloxy then the acylamino or acyloxy group does not carry an aryl, substituted aryl, heteroaryl or substituted heteroaryl group;

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

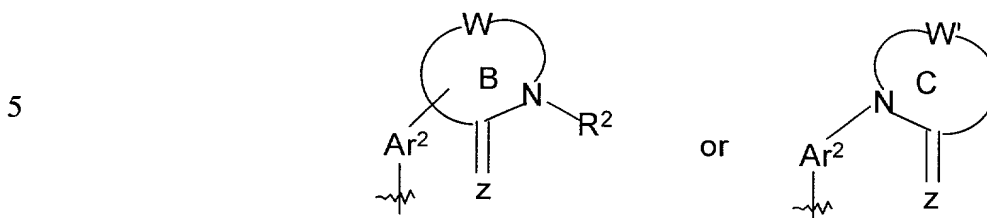
11. The compound of Claim 10 wherein Ar¹ is phenyl, pyridinyl, or pyrimidinyl ring.

12. The compound of Claim 11 wherein R⁹ is selected from the group consisting of -O-Z^a-NR¹¹R^{11'} and -O-Z^a-R¹² wherein R¹¹ and R^{11'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, and where R¹¹ and R^{11'} are joined to form a heterocycle or a substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z^a is selected from the group consisting of -C(O)- and -SO₂-.

13. The compound of Claim 12 wherein R⁹ is -OC(O)NR¹¹R^{11'}.

14. The compound of Claim 13 wherein X is hydroxy and R¹, R³ and R^{3a} are hydrogen and R⁹ is -OCON(CH₃)₂.

15. The compound of Claim 1 wherein R^{2a} is a group of formula (a) or (b):



wherein Ar^2 , B, C and Z are as defined above.

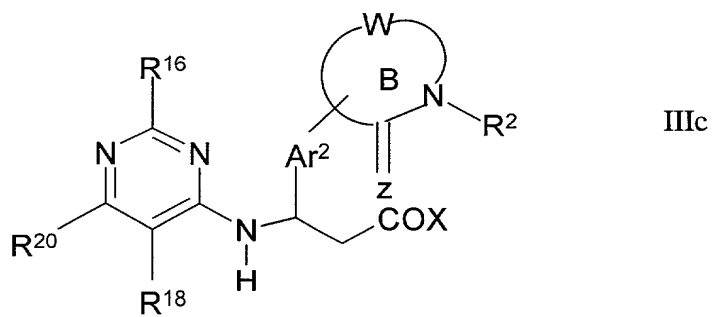
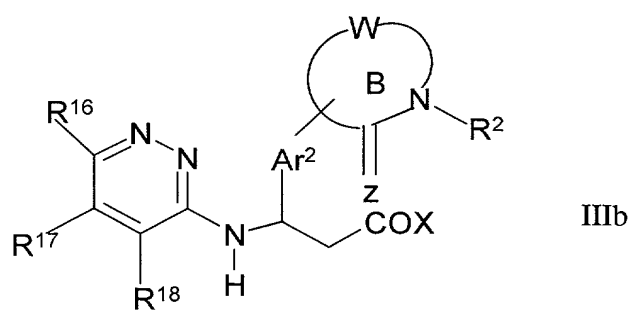
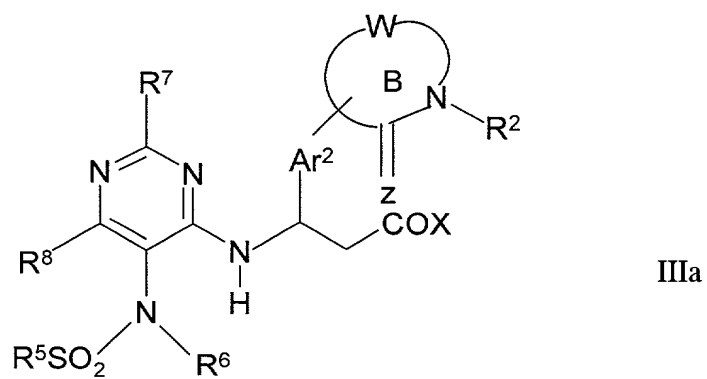
16. The compound of Claim 15 wherein B is either:

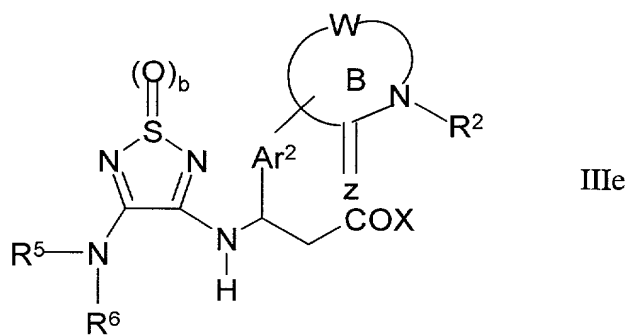
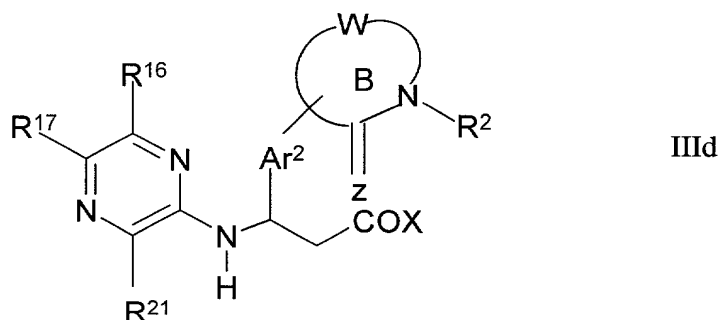
(a) a group wherein W, together with $-C(=Z)NR^2-$ where Z is $-O-$, forms an unsaturated heterocyclic group containing 3 or 4 carbon atoms and 0 or 1 additional nitrogen atoms and further the wherein the unsaturated heterocyclic group is optionally substituted, in addition to the R^2 group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino; or

(b) a group wherein W, together with $-C(=Z)NR^2-$ where Z is $-O-$, forms a saturated or unsaturated heterocyclic group containing 3 or 4 carbon atoms and 0 or 1 additional nitrogen atoms wherein said saturated or unsaturated heterocyclic group is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one and wherein the resulting fused ring is optionally substituted, in addition to the R^2 group, on any ring atom capable of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino; and

C is either:

- (a) a group wherein W, together with $-C(=Z)NR^2-$ where Z is -O-, forms an unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and further the wherein the unsaturated heterocyclic group is optionally substituted, in addition to the R^2 group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino; or
- (b) a group wherein W, together with $-C(=Z)NR^2-$ where Z is -O-, forms a saturated or unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms wherein said saturated or unsaturated heterocyclic group is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one and wherein the resulting fused ring is optionally substituted, in addition to the R^2 group, on any ring atom capable of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.
17. The compound of Claim 16 wherein R^1 , R^3 and R^{3a} are hydrogen, and X is preferably hydroxy.
18. The compound of Claim 1 wherein the compounds has the formula IIIa, IIIb, IIIc, IIId, or IIIE:





wherein:

X is hydroxyl or alkoxy;

Ar² is an aryl or heteroaryl group optionally substituted, in addition to
 20 ring B or C, with one or two substituent(s) selected from the group consisting
 of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy,
 substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino,
 substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-
 alkylamino, substituted N-acyl-N-alkylamino, (alkylsulfonyl)amino,
 25 substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-alkylamino, substituted
 N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl,
 substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted
 cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl,
 carboxy, substituted carboxy, thiol, alkylthio, substituted alkylthio,

alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, and substituted alkylsulfonyl;

5 R⁵ is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

10 R⁶ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and -SO₂R¹⁰ where R¹⁰ is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

15 R⁷ and R⁸ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

20 R¹⁶ and R¹⁷ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

25 R¹⁸ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

30 R²⁰ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

R²¹ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2; and

- 5 B is a group wherein W, together with -C(=Z)NR²-, forms a saturated or unsaturated heterocyclic group containing 2 to 5 carbon atoms and 0 to 4 additional heteroatoms selected from the group consisting of nitrogen, oxygen, and -SO_n- (where *n* is 0 to 2) wherein said saturated or unsaturated heterocyclic group is optionally fused with one or two ring(s) structures
- 10 selected from the group consisting of cycloalkyl, cycloalkenyl, heterocyclic, aryl and heteroaryl group to form a bi- or tri-fused ring system and further wherein said heterocyclic group and each of such ring structures are optionally substituted with 1 to 3 substituents selected from the group consisting of with one or two substituent(s) selected from the group consisting
- 15 of hydrogen, halogen, hydroxy, alkoxy, substituted alkoxy, acyloxy, substituted acyloxy, amino, alkylamino, substituted alkylamino, dialkylamino, substituted dialkylamino, acylamino, substituted acylamino, N-acyl-N-alkylamino, substituted N-acyl-N-alkylamino, alkylenedioxy, (alkylsulfonyl)amino, substituted (alkylsulfonyl)amino, N-(alkylsulfonyl)-N-
- 20 alkylamino, substituted N-(alkylsulfonyl)-N-alkylamino, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, cyano, acyl, substituted acyl, carboxy, substituted carboxy, nitro, thiol, alkylthio, substituted alkylthio, alkylsulfoxy, substituted alkylsulfoxy, alkylsulfonyl, substituted alkylsulfonyl, aryl, substituted aryl, heteroaryl, substituted
- 25 heteroaryl;

R² is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, and substituted cycloalkenyl; and

and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

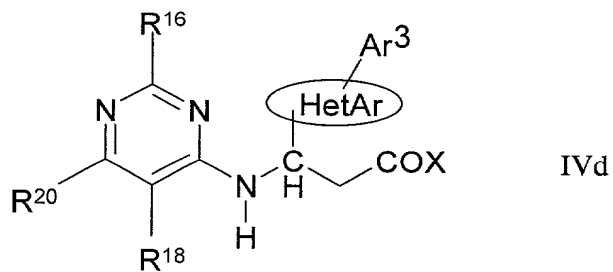
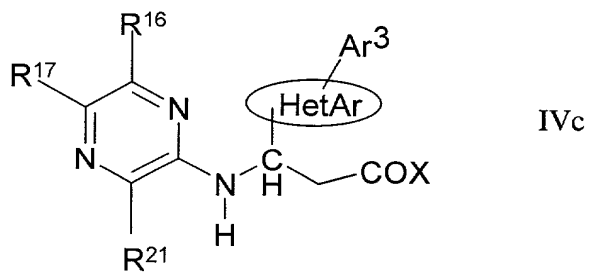
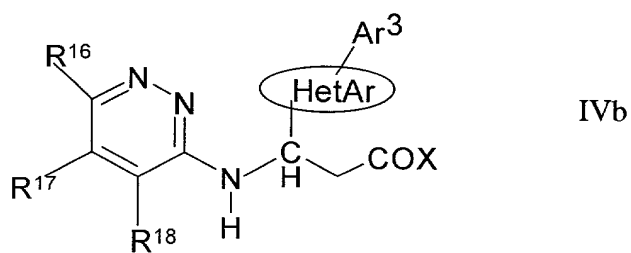
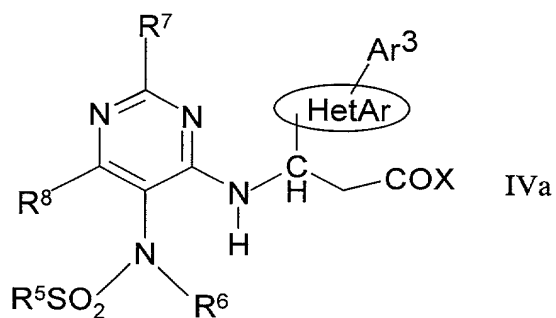
19. The compound of Claim 18 wherein B is either:

- 5 (a) a group wherein W, together with $-C(=Z)NR^2-$ where Z is $-O-$, forms an unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms and further the wherein the unsaturated heterocyclic group is optionally substituted, in addition to the R^2 group, with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or
- 10 dialkylamino; or
- (b) a group wherein W, together with $-C(=Z)NR^2-$ where Z is $-O-$, forms a saturated or unsaturated heterocyclic group containing 2 to 4 carbon atoms and 0 to 2 additional nitrogen atoms wherein said saturated or unsaturated
- 15 heterocyclic group is fused to a heterocyclic ring selected from the group consisting of dioxolane, dioxane, homodioxane, oxetane, tetrahydrofuran, dihydropyran, furan, oxazolidine, oxazole, isoxazole, oxazolidinone, oxathiolane, and 1,3-dioxolan-2-one and wherein the resulting fused ring is optionally substituted, in addition to the R^2 group, on any ring atom capable
- 20 of substitution with 1 or 2 substituents selected from the group consisting of alkyl, alkoxy, substituted alkoxy, alkenyloxy, substituted alkenyloxy, halo, hydroxy, mono or dialkylamino.

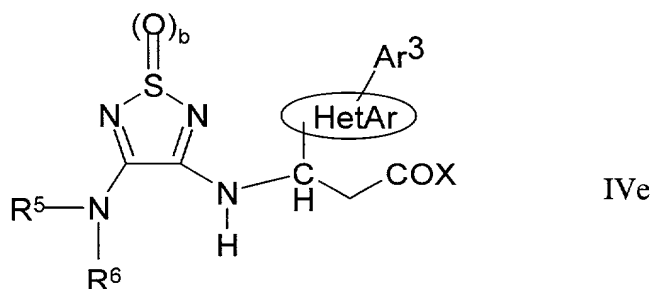
20. The compound of Claim 19 wherein Ar^2 is preferably phenyl.

21. The compound of Claim 1 wherein R^{2a} is HetAr where HetAr is a nitrogen containing 6- membered heteroaryl that is optionally substituted with an aryl or substituted aryl group.

22. The compound of Claim 1 wherein the compounds are of formula IVa, IVb, IVc, IVd, or IVe:



5



wherein:

HetAr is a nitrogen containing heteroaryl group;

10 Ar³ is aryl or substituted aryl;

R⁵ is selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

15 R⁶ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and -SO₂R¹⁰ where R¹⁰ is selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl;

20

R⁷ and R⁸ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

25

R¹⁶ and R¹⁷ are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen; and

30

R¹⁸ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic and substituted heterocyclic;

5 R²⁰ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and halogen;

10 R²¹ is selected from the group consisting of alkyl, substituted alkyl, alkoxy, substituted alkoxy, amino, substituted amino, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclic and substituted heterocyclic;

b is 1 or 2; and

X is hydroxyl; and

15 and enantiomers, diastereomers and pharmaceutically acceptable salts thereof.

23. The compound of Claim 22 wherein HetAr is pyridinyl, pyrimidinyl, pyrazinyl, or pyridazinyl and Ar³ is substituted phenyl.

20 24. A method for treating a disease mediated by VLA-4 in a patient, which method comprises administering a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 1-23.

25 25. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of Claim 1-23.

26. A method for binding VLA-4 in a biological sample which method comprises contacting the biological sample with a compound of Claim 1
30 under conditions wherein said compound binds to VLA-4.